

ORIGINAL ARTICLE

Effects of consuming a high-protein diet with or without soy protein during weight loss and maintenance: a non-inferiority, randomized clinical efficacy trial

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[Correction added on 02 July, 2018, after first online publication: the affiliation of M.R. Flock has been corrected to "Clinical & Translational Science Institute, University of Pittsburgh, Pittsburgh, PA, USA"].

Summary

Objective

This 12-month randomized, non-inferiority clinical trial sought to determine the impact of consuming soy protein as part of an energy-restricted, high-protein diet on weight loss, body composition and cardiometabolic health.

Methods

Seventy-one adults (58 female) with overweight or obesity (body mass index: $32.9 \pm 3.6 \text{ kg m}^{-2}$) were randomly assigned to consume three servings of soy (S) or non-soy (NS) protein foods per day for 12 months. All participants completed a group-based behavioural weight loss program lasting 4 months (M4), and follow-up assessments were completed at month 12 (M12).

Results

Body weight was reduced in both groups at M4 (S: $-7.0\% \pm 5.2\%$, NS: $-7.1\% \pm 5.7\%$) and M12 (S: $3.6\% \pm 5.1\%$, NS: $-4.8\% \pm 7.3\%$). Body weight reductions (mean difference [90% confidence interval]) were not different between S and NS at either time point (M4: $-0.16\% [-1.4, 3.6]$, $P = 0.90$; M12: $1.1\% [-1.4, 3.6]$, $P = 0.44$). Differences in body fat mass loss were not different between S and NS at M4 ($0.29 \pm 0.84 \text{ kg}$, $P = 0.73$) or M12 ($0.78 \pm 1.5 \text{ kg}$, $P = 0.59$). Weight loss-induced improvements in cholesterol, triglycerides and blood pressure did not differ between S and NS.

Conclusion

These results indicate that soy-based protein foods can be effectively incorporated into an energy-restricted, high-protein diet for improving body weight, body composition and cardiometabolic health.

Keywords: Body composition, dietary protein, obesity, weight loss.

Introduction

Higher protein (HP) diets may help with weight loss by increasing satiety, increasing energy expenditure and promoting greater loss of fat vs. fat-free mass compared with lower or normal protein diets that provide dietary protein at or near the current Recommended Daily Allowance of 0.8 g of protein per kg of body weight (1–4). It was previously reported that a HP diet that included lean beef was as effective as a HP diet without beef in producing

weight loss while preserving fat free mass and improving cardiometabolic health (5). Whether weight loss is impacted by the source of protein has not been exhaustively studied, and some evidence indicates that proteins from animal vs. plant sources may differentially impact appetite and eating behaviour (6).

Some previous studies have investigated the impact of animal vs. plant-based HP diets on weight loss, appetite and ingestive behaviour, and cardiovascular disease risk factors (7–10). In general, findings from these studies

support a broadly beneficial impact of HP diets with limited differences between animal-based and plant-based diets (7). Interest in plant-based diets, however, is on the rise as evidenced by the 2015–2020 Dietary Guidelines for Americans, which call for an increase in the consumption and variety of vegetables and protein foods including soy products (11). Therefore, more studies are warranted to investigate the potential impact of using non-animal protein sources to meet dietary protein intakes, especially for HP diets for weight loss. Such findings would provide individuals with greater dietary flexibility for following HP diets, which are common for weight management.

Soy foods are a uniquely rich source of high quality protein and bioactive plant compounds that have been studied for their association with cardiometabolic health ranging from improvements in blood lipid profiles to preferential reductions in body fat (12–15). Short-term studies have also found that soy proteins elicit similar satiety and appetite-related hormone responses as animal-based proteins (6), which supports the potential role of consuming soy proteins as part of a HP diet for weight loss. Limited data, however, are available concerning the impact of HP diets containing large amounts of soy on weight loss and its effects on key biomarkers of cardiometabolic health. Soy protein represents a potentially attractive plant-based protein for research because it is generally regarded as the highest quality plant protein (16). This research is particularly important for vegetarians and/or vegans, who may experience greater difficulty in adhering to HP diets due to fewer dietary protein options compared with those following an omnivorous diet. The primary aim of this trial was to evaluate and compare the effectiveness of incorporating soy protein-based foods compared with other proteins into high-protein diets for weight loss. Secondary aims were to assess whether soy protein foods consumed as part of an energy-restricted, HP diet influenced changes in body composition or cardiometabolic health.

Unlike trials designed to test superiority of a treatment compared with a placebo or control group, non-inferiority trials are designed to test the comparative effectiveness of a new intervention or treatment and established intervention or treatment options (17). Increasing emphasis has been placed on the use of non-inferiority designs because assigning patients to a placebo can often be unethical, costly and potentially unnecessary given the research question at hand. This study was thus designed as a non-inferiority trial to evaluate and compare two active dietary treatment arms for their effectiveness in promoting weight loss. It was hypothesized that weight change at the end of a 4-month comprehensive weight loss program would not differ (defined by a non-inferiority

margin of $\Delta \leq 3\%$) between HP diets with soy or non-soy proteins.

Methods

Participants

Eighty-five individuals were recruited from the Denver, CO metropolitan area to participate in this randomized weight loss trial. Participants were first screened by phone based on the following inclusion criteria: men and women aged 18–55 years, body mass index (BMI) 27–40 kg m⁻², weight stable ($\Delta \leq 4.5$ kg in last 3 months), generally healthy, able to progress in an exercise program up to 70 min 6 d per week at a moderate intensity. Subjects also had to be willing and able to participate in group classes held once per week for 16 consecutive weeks and willing to participate in five study visits (screening, baseline, month 4 [M4], month 8 and month 12 [M12]) over the study period. All study visits and group weight loss classes were conducted at the University of Colorado Anschutz Health and Wellness Center in Aurora, CO, between February 2015 and October 2016. All protocols were reviewed and approved by the Western Institutional Review Board (Olympia, WA). Participants provided written informed consent and received a monetary stipend for participating in the study.

Experimental design

A non-blinded, two-arm, block randomized controlled trial was used to investigate the relative efficacy of consuming soy vs. non-soy protein foods as part of a HP diet consumed during 4 months of voluntary weight loss and 8 months of weight loss maintenance. All participants participated in the *State of Slim* (SOS) weight management program, which is a 16-week group-based, lifestyle modification program (5,18). The SOS program consisted of weekly classes of 20 participants that were stratified by diet assignment. A copy of the SOS book and access to the online SOS community were provided to all participants. Participants were randomly assigned to one of two experimental diets: a HP including three daily soy protein products (S) or a HP diet that was restricted in soy protein products (NS).

Diet intervention

The SOS diet plan is HP, low in fat and emphasizes non-starchy (i.e. vegetable) and whole-grain carbohydrates. Protein foods throughout the entire SOS program are lean and minimally processed (i.e. lean meat and poultry, fish, egg whites and fat-free dairy). The diet plan is structured

into three distinct phases with phase-specific food choices from which participants can choose to eat in defined portions rather than counting calories. Prescribed food lists, portion sizes for the SOS diet plan and additional details of the SOS weight management program have been published previously (5). All participants were provided with a SOS book and instructed to select foods from the list for each diet phase with additional group-specific instructions as described in the succeeding texts. Participants assigned to S were provided with three pre-made, soy protein food products to consume each day for the duration of the 12-month study period. These soy products consisted of a packet of protein powder, a protein bar and a frozen protein patty (similar to a sausage patty). The SOS program recommends consuming a five to six meals per day with a serving at each meal. Thus, participants assigned to S were given enough soy protein products to provide 50–60% of their prescribed daily protein intake. The remaining 40–50% of dietary protein was to be self-chosen from the SOS food lists provided in the book, which includes both animal-based and vegetarian dietary protein options. Participants assigned to NS were asked to consume three servings of self-selected soy-free protein products each day for the duration of the study period. NS participants were given monetary stipends at baseline, M4 and month 8 study visits to purchase soy-free, SOS-approved protein powders and bars.

Following the completion of the 16-week SOS program and M4 testing day, participants initiated the 8-month weight loss maintenance phase of the study. The following recommendations for weight loss maintenance were given during weeks 15 and 16 of the SOS program: (1) eat high quality foods most of the time (i.e. follow Phase 3 of the dietary program 80% of the time); (2) keep your activity level high (i.e. 70 min d⁻¹ and 6 d week⁻¹); (3) weigh yourself every day; (4) set a 'take action' weight (i.e. a weight at which one would re-engage weight loss efforts); and (5) be a role model. No additional touchpoints or interventions were made during the maintenance period of the study outside of on-site study assessments at months 8 and 12 and the in-person distribution of additional soy products at months 6 and 10.

Because the hypothesis was that weight loss would be similar between the S and NS groups, a non-inferiority research design was used. The primary outcome was change in body weight at the end of weight loss (M4). A non-inferiority margin of 3% was set for the upper bound of the confidence interval (CI) for the mean difference in per cent weight loss between the two study arms (soy–non-soy). This margin was chosen based on variation seen in delivering SOS weight management programs to over 1,000 subjects over the past 18 months. Differences

in the taste, product selection and appearance of recommended and/or supplied protein sources precluded blinding the study. Secondary outcomes included weight loss maintenance at M12 and changes in body and trunk composition, blood glucose, blood urea nitrogen (BUN), C-reactive protein (CRP), lipids, blood pressure and physical activity (total metabolic equivalents [METs] per week) at M4 and M12. This study was registered on ClinicalTrials.gov (NCT02380963).

Dietary compliance

Body weight, total daily protein consumption (average number of protein servings per day) and supplemental protein consumption (average number of supplemental soy or non-soy protein servings per day) were used to collectively assess adherence to the dietary protocol. Protein consumption was tracked via daily dietary recall logs collected weekly during the 4-month weight loss phase and twice during the maintenance phase (months 8 and 12). Compliance data are summarized as total protein servings per week and total soy protein servings per week compared between groups for total protein and cohorts for soy protein. Fasting BUN is known to change with altered protein intakes (19) and was used as a crude marker of dietary protein consumption to corroborate self-reported protein intake.

Body weight and composition

Fasting body weight was assessed in light clothing, with no shoes using a Befour PS6600 calibrated digital scale (Befour, Inc., Saukville, WI, USA). Body composition and body fat distribution were assessed via dual X-ray absorptiometry using a Hologic Discovery QDR Series unit running APEX software version 4.5 (Hologic, Bedford, MA, USA).

Blood pressure

Blood pressure was assessed manually using a sphygmomanometer. Subjects were asked to sit for 5 min prior to the reading, and measurement was taken with legs uncrossed. The back and arm were supported during the measurement, and the same arm was used at each study visit.

Blood analyses

Blood samples were collected in the fasted state during each on-site assessment and analysed for a basic metabolic panel (including glucose and BUN), CRP and lipids. For the baseline and M4 study visits, lipids were

measured using the Vertical Auto Profile (VAP) test that provided direct analysis of lipoproteins via vertical density-gradient ultracentrifugation followed by the assessment of cholesterol distribution (Atherotech, Birmingham, AL, USA) (20). The VAP method was substituted with the LipoProfile nuclear magnetic resonance spectroscopy test (ARUP Laboratories, Salt Lake City, UT, USA) for subsequent study visits due to a manufacturer discontinuation of the patented VAP procedure in February of 2016.

Per the appropriate testing protocol, blood samples were collected into red top 6 mL CAT tubes or gold top 5 mL SST tubes, allowed to clot for 60 min at room temperature and centrifuged for 15 min at 1.3 relative centrifugal force and 20°C. Samples for obtaining plasma were collected in heparin-containing 4.5 mL PST tubes and immediately spun for 15 min at 2.2 relative centrifugal force and 20°C. All blood samples were analysed at the University of Colorado Hospital Authority Clinical Laboratory in Aurora, CO.

Physical activity

Physical activity levels were assessed as total METs of task per week using the International Physical Activity Questionnaire (IPAQ). The validated long format of the IPAQ is designed to assess self-reported physical activity across six activity domains (occupational, transport, yard/garden, household, leisure/volitional exercise and sitting). Self-reported pace is reported as an estimate of exercise intensity, which is then used to convert reported activity minutes into MET estimates (21).

Statistical analyses

Study data were collected and managed using REDCap electronic data capture tools hosted at University of Colorado – Anschutz Medical Campus. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources (22).

This study was powered on the intent-to-treat (ITT) analysis of detecting non-inferiority of soy protein foods to non-soy protein foods with an *a priori* non-inferiority margin of $\Delta \leq 3\%$ for relative weight change. To detect non-inferiority using a one-sided test, a sample size of 30 participants per arm was indicated for 80% power at 5% significance. For ease of clinical interpretation, the

change from baseline at M4 (weight loss) and M12 (maintenance) was used as the primary and secondary end points for efficacy assessment. Separate analyses were performed for the weight loss (M4 – baseline) period and maintenance (M12 – M4) periods. All data and analyses presented represent the ITT condition. For the ITT analysis, baseline-observation-carry-forward was used for missing M4 and 12 end points. A 90% two-sided CI for the mean difference between the soy and non-soy groups was calculated at the end of M4 and M12. If the upper bound of the CI was smaller than the pre-specified non-inferiority margin of $\Delta \leq 3\%$, non-inferiority would be established and followed by a test for superiority using the ordinary null value. For the superiority test, the minimum detectable effect sizes were 0.63 common standard deviations for comparing two groups. Because secondary outcomes were not part of the *a priori* hypothesis, no adjustment for multiple comparisons was made (23,24). All *P*-values are reported. Descriptive data are presented as mean \pm standard deviation and outcomes data as mean \pm standard error.

To delineate the profile of change in outcome variables over the entire study period, a linear mixed effects model was fit, as supportive analyses, to all the data points of the primary and secondary outcomes with repeated measures. Independent variables in this model consisted of the measuring time and dietary treatment indicator as classification variables and their interaction term. Unstructured covariance was used in all the mixed model analyses. Time by group interaction, within-group change between different time points and between-group difference at different time points were tested using contrasts.

Results

Study recruitment and retention

Shown in Figure 1, a total of 85 individuals were screened for this study. Seventy-two of the 85 met the inclusion criteria and were enrolled. One participant withdrew from the study prior to randomization for a total of 71 participants. Thirty-six participants were randomized to the soy group and 35 to the non-soy group. Of the 71 participants enrolled, 80.3% (soy: $n = 29$; non-soy: $n = 28$) completed the weight loss phase (baseline – M4) and 63.4% (soy: $n = 21$; non-soy: $n = 24$) completed the entire trial (baseline – M12). During the weight loss intervention, 2 were lost to follow up (from the soy group) and 12 withdrew consent (five from the soy group and seven from the non-soy group) with the reasons for dropout being family, work and time commitment issues ($n = 7$), rigour/difficulty of the SOS intervention ($n = 2$), dislike of the supplemental soy products ($n = 2$) and moving out

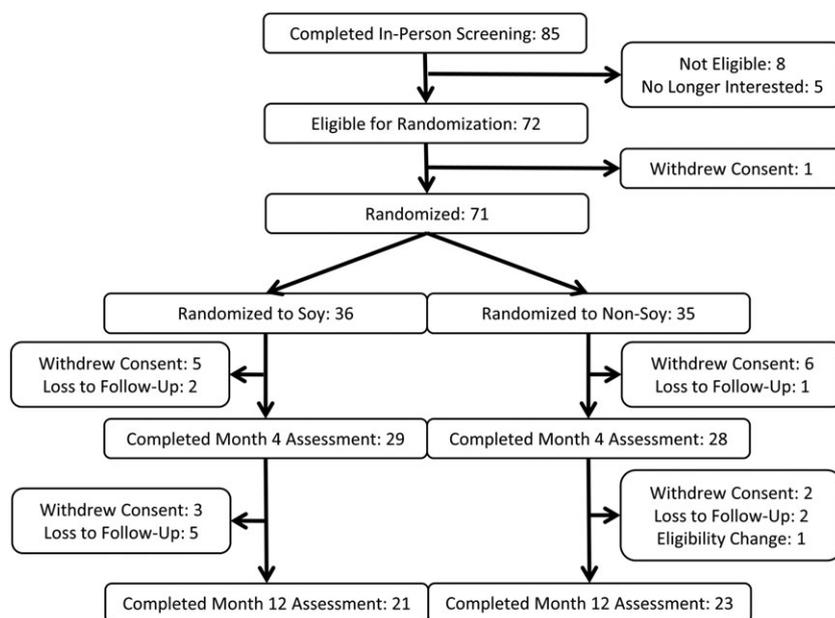


Figure 1 Participant recruitment diagram.

of state ($n = 1$). During the maintenance phase, seven were lost to follow up (six from the soy group and one from the non-soy group), one was withdrawn due to pregnancy (from the non-soy group) and four withdrew consent (two from soy and two from non-soy). Dropouts during this time were due to loss of interest/desire to continue the program ($n = 2$) and time commitment issues ($n = 2$).

Participant characteristics

Baseline demographics and physical characteristics of the 71 individuals randomized in the study (Table 1) were similar between intervention groups with the exception of diastolic blood pressure, which was significantly higher in the soy group (soy: 77.9 ± 7.5 mmHg; non-soy, 73.9 ± 8.5 mmHg, $P = 0.04$). Participants were, on average, 42 ± 9 years old with a BMI of 32.9 ± 3.5 , and 82% of the participants were women. Baseline blood parameters, blood pressure and physical function tests were reflective of a healthy participant sample.

Dietary compliance

Compliance was assessed based on self-reported total protein servings per day and average supplemental protein consumption per day (100% compliance = 3 servings per day) for the weight loss (112 d) and maintenance (252 d) phases of the study. Self-reported compliance to

Table 1 Baseline participant characteristics¹

Parameter	Soy ($n = 35$)	Non-soy ($n = 36$)
Age (years)	42.4 ± 10.7	41.8 ± 7.9
Female ($n, \%$)	29 (80.6%)	29 (82.9%)
Body weight (kg)	94.9 ± 14.3	90.6 ± 11.4
BMI (kg m^{-2})	33.1 ± 3.5	32.7 ± 3.6
Body fat (%)	39.7 ± 7.2	40.2 ± 5.6
Glucose (mg dL^{-1})	95.4 ± 11.2	92.2 ± 8.2
Total cholesterol (mg dL^{-1})	196.3 ± 41.9	196.9 ± 43.4
LDL (mg dL^{-1})	119.1 ± 33.7	119.9 ± 35.2
HDL (mg dL^{-1})	53.7 ± 13.0	55.9 ± 11.2
Triglycerides (mg dL^{-1})	123.2 ± 57.8	112.4 ± 39.2
Systolic BP (mmHg)	115.7 ± 11.9	111.2 ± 11.4
Diastolic BP (mmHg)	77.9 ± 7.5	73.9 ± 8.5
CRP (mg L^{-1})	7.7 ± 8.8	4.8 ± 4.0
Physical activity (MET per week)	56.0 ± 41.7	62.9 ± 41.7

¹All values are mean \pm standard deviation.

BMI, body mass index; BP, blood pressure; CRP, C-reactive protein; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; MET, metabolic equivalent.

the high-protein dietary protocol (100% compliance = 6 servings per day) was also similar between groups during the weight loss (soy: 5.2 ± 0.5 servings per day, $n = 32$; non-soy: 5.1 ± 0.5 servings per day, $n = 34$) and maintenance phases (soy: 5.2 ± 0.7 servings per day; non-soy: 4.2 ± 1.3 servings per day). Consumption of supplemental protein foods (100% compliance = 3 servings per day) in the soy group averaged 2.4 ± 0.7 servings per day during

weight loss and 2.5 ± 0.5 servings per day during the maintenance phase; consumption in the non-soy group averaged 2.2 ± 0.04 servings per day during weight loss and 1.9 ± 0.07 servings per day during the maintenance phase. Completion rate of the food logs was determined by number of daily logs received divided by total days in each phase. Completion rates were as follows: soy: $63.9\% \pm 31.2\%$; non-soy group $65.1\% \pm 35.9\%$ during the weight loss phase; and soy: $54.7\% \pm 35.9\%$; non-soy: $62.5\% \pm 35.1\%$ during the maintenance phase.

In accordance with the HP diet, BUN levels were significantly and similarly increased by 3.5–4.0 mg dL⁻¹ from baseline values of 13.8 mg dL⁻¹ in both of the groups at M4, and 2.7–3.5 mg dL⁻¹ at M12. No differences were observed between groups in the amount of change seen between BUN levels at M4 or M12.

Changes in body weight and body mass index

Absolute (kg) and relative (%) changes in body weight at the end of M4 and M12 for each of the treatment groups

are shown in Table 2. Both groups lost significant and similar amounts of body weight at each time point. Relative to the *a priori* non-inferiority margin of 3% (Figure 2), the 90% CIs for the difference in absolute and relative weight change between groups at the end of the weight loss intervention (M4) were $-2.3, 1.8$ kg ($P = 0.84$) and $-2.0, 2.3\%$ ($P = 0.90$), respectively. BMI was reduced at M4 (S: -2.9 ± 0.3 kg m⁻², NS: -2.9 ± 0.3 kg m⁻², both $P < 0.001$) and at M12 (S: -1.5 ± 0.5 kg m⁻², $P = 0.002$, NS: -2.0 ± 0.5 kg m⁻², $P < 0.001$) with no differences in BMI reduction between N and NS (P value for difference at M4 = 0.98 and M12 = 0.40).

Changes in body composition

Table 3 shows the changes in body fat %, fat mass and lean mass at M4 and M12. Both groups lost significant amounts of lean and body fat mass at the end of the weight loss intervention (M4). No statistical differences or overall interactions were observed between the groups

Table 2 Mean difference in weight loss at month 4 and month 12 between soy and non-soy

Outcome	Time point	Soy	Non-soy	Group differences	
				Δ (90% CI)	P value
Weight change (kg)	Month 4	-6.6 ± 5.0	-6.4 ± 5.1	-0.24 ($-2.3, 1.8$)	0.84
	Month 12	-3.4 ± 5.0	-4.2 ± 6.6	0.75 ($-1.6, 3.1$)	0.59
Weight change (%)	Month 4	-7.0 ± 5.2	-7.1 ± 5.7	0.16 ($-2.0, 2.3$)	0.90
	Month 12	-3.6 ± 5.1	-4.8 ± 7.3	1.1 ($-1.4, 3.6$)	0.44

Results are presented as mean weight change \pm standard error and mean difference in weight change with 90% confidence intervals (CIs) using an intention to treat analysis. P value is from two-tailed Student's t -test for testing the null hypothesis that mean group difference is zero.

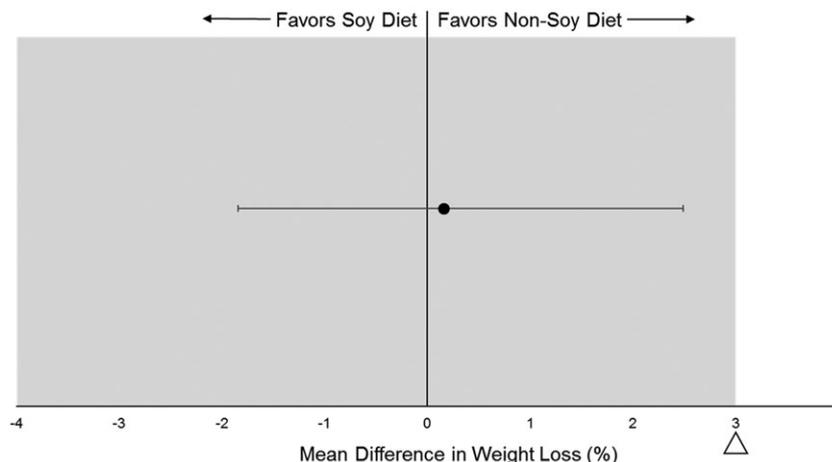


Figure 2 Mean difference in relative weight loss (%) between soy and non-soy groups relative to the 3% non-inferiority margin. The intention to treat analysis indicated similar % weight loss at month 4 between soy and non-soy.

Table 3 Changes in body composition at month 4 and month 12¹

Outcome variable	Group	Time point			Month 4 – baseline	P value	Month 12 – baseline	P value
		Baseline	Month 4	Month 12				
Total body fat mass (kg)	Soy	37.1 (1.4)	30.7 (1.4)	33.0 (1.7)	–6.4 (0.6)	<.001	–4.1 (1.0)	<.001
	Non-soy	35.7 (1.4)	29.0 (1.5)	30.8 (1.7)	–6.7 (0.6)	<.001	–4.9 (1.0)	<.001
	Difference	1.4 (2.0)	1.7 (2.0)	2.2 (2.4)	0.3 (0.8)	0.732	0.8 (1.5)	0.592
Total body fat (%)	Soy	39.7 (1.1)	36.0 (1.2)	36.5 (1.2)	–3.8 (0.5)	<.001	–3.2 (0.6)	<.001
	Non-soy	40.2 (1.2)	35.6 (1.2)	36.4 (1.2)	–4.6 (0.5)	<.001	–3.9 (0.5)	<.001
	Difference	–0.5 (1.6)	0.3 (1.7)	0.1 (1.7)	0.8 (0.7)	0.246	0.6 (0.8)	0.429
Total body lean mass (kg)	Soy	55.8 (1.5)	54.2 (1.6)	55.6 (1.6)	–1.6 (0.3)	<.001	–0.18 (0.4)	0.668
	Non-soy	53.0 (1.5)	51.9 (1.6)	52.6 (1.6)	–1.1 (0.3)	<.001	–0.48 (0.4)	0.24
	Difference	2.7 (2.2)	2.2 (2.3)	3.0 (2.3)	–0.48 (0.4)	0.286	0.30 (0.6)	0.609

¹Intention to treat linear mixed-effects model analysis with unstructured covariance was used to assess the efficacy of intervention on each outcome variable (soy: $n = 36$; non-soy: $n = 35$). Test of time by group interaction was used to test the efficacy of intervention at each time point. Results are mean (standard error). Significant P values ($P < 0.05$) are indicated in bold.

for any of the body composition variables at any point in the trial.

Changes in cardiometabolic health and physical activity

Intervention and dietary treatment effects on metabolic, cardiovascular and physical activity measures are shown in Table 4. Lipids and blood pressure were similarly reduced and physical activity similarly increased between groups at the end of M4. Briefly, low-density lipoprotein cholesterol was reduced by an average of 16 mg dL^{-1} , total cholesterol by 22 mg dL^{-1} , triglycerides by 37 mg dL^{-1} and systolic and diastolic blood pressure by 4 mmHg; self-reported physical activity increased by 15 METs per week. Although there were no significant differences or overall interactions between the groups for any of the outcome measures, CRP was significantly reduced at M4 and M12 in S only ($P < 0.05$). Triglycerides, on the other hand, remained significantly reduced at the end of the trial only in NS, while total cholesterol remained reduced in both groups at the end of M12. Glucose and high-density lipoprotein concentrations were not changed in either of the groups at any point in the trial.

Discussion

As hypothesized, similar weight loss was observed between HP, energy-restricted diets with either supplemental soy-protein based foods or non-soy-based proteins. The difference between groups was within a predetermined non-inferiority margin of $\Delta \leq 3\%$ for relative change in body weight following 4 months of volitional weight loss. Both groups experienced similar improvements in secondary outcomes such as body composition, lipids and blood pressure. Some weight

regain occurred during the self-directed, 8 month follow-up period, but there were no significant differences between the dietary treatment groups for any of the outcome measures throughout the 12-month trial. While not a fully vegetarian diet, these findings are encouraging for vegetarians who struggle to consume sufficient amounts of dietary protein and for those seeking to add lean sources of high quality plant proteins to their diets for optimal health and weight management.

A wide range of health benefits is associated with weight loss in overweight and obese adults; however, a potential drawback of weight loss can be the accompanying loss of skeletal muscle mass (3). Although this study was not powered to investigate changes in body composition and lacked a standard protein diet group, it is worth noting that, in contrast to the composition of weight loss observed at M4 (7.8 kg, 83% body fat mass, 17% lean mass) the composition of weight loss at the end of M12 (–4.6 kg) consisted of 95% body fat and 5% lean mass (Table 4). Importantly, IPAQ reported increases in physical activity at both time points did not differ between groups suggesting that differences in physical activity in terms of total METs per week did not contribute towards the outcome results; however, we did not collect detailed information on exercise type and frequency. While speculative, these data warrant further investigation as they suggest that a HP diet may have beneficial effects on the composition of weight re-gain.

Interest in plant-based diets has increased with the latest dietary recommendations to consume more vegetables and plant-based foods high in protein such as soy (11,25). The protein digestibility-corrected amino acid scores (the most widely recognized and approved method for evaluating protein quality) for soy protein are comparable with milk, meat and eggs making it the highest quality of all the plant proteins (16). Soy protein

Table 4 Changes in markers of cardiometabolic health at month 4 and month 12¹

Outcome variable	Group	Time point			Month 4 – baseline	P value	Month 12 – baseline	P value
		Baseline	Month 4	Month 12				
Glucose (mg dL ⁻¹)	Soy	95.4 (1.6)	95.3 (1.2)	94.1 (1.4)	-0.2 (1.5)	0.915	-1.3 (1.3)	0.298
	Non-soy	92.2 (1.7)	91.9 (1.2)	91.3 (1.3)	-0.3 (1.5)	0.862	-0.9 (1.2)	0.445
	Difference	3.2 (2.3)	3.3 (1.7)	2.8 (1.9)	0.1 (2.1)	0.961	-0.4 (1.8)	0.825
BUN (mg dL ⁻¹)	Soy	13.9 (0.5)	17.4 (0.8)	16.7 (0.8)	3.5 (0.8)	<.001	2.7 (0.8)	<.001
	Non-soy	13.7 (0.5)	17.7 (0.8)	17.2 (0.8)	4.0 (0.8)	<.001	3.5 (0.7)	<.001
	Difference	0.2 (0.7)	-0.3 (1.1)	-0.6 (1.1)	-0.5 (1.1)	0.667	-0.8 (1.1)	0.455
CRP (mg L ⁻¹)	Soy	7.7 (1.2)	5.0 (0.8)	5.4 (1.0)	-2.7 (1.0)	0.006	-2.3 (0.8)	0.003
	Non-soy	4.8 (1.2)	4.0 (0.9)	3.4 (1.0)	-0.8 (1.0)	0.395	-1.4 (0.8)	0.069
	Difference	2.9 (1.7)	1.0 (1.2)	2.0 (1.4)	-1.9 (1.4)	0.177	-0.9 (1.1)	0.401
LDL-C (mg dL ⁻¹)	Soy	119.2 (5.7)	105.1 (5.0)	104.9 (5.7)	-14.1 (3.9)	<.001	-14.3 (4.8)	0.004
	Non-soy	119.9 (5.8)	101.1 (5.1)	111.0 (5.7)	-18.9 (3.9)	<.001	-8.9 (4.7)	0.062
	Difference	-0.7 (8.2)	4.0 (7.2)	-6.1 (8.1)	4.7 (5.6)	0.401	-5.4 (6.7)	0.421
HDL-C (mg dL ⁻¹)	Soy	53.6 (2.0)	52.9 (1.7)	52.3 (2.2)	-0.7 (1.3)	0.63	-1.2 (1.5)	0.417
	Non-soy	54.9 (2.0)	52.7 (1.7)	53.1 (2.2)	-2.2 (1.3)	0.104	-1.8 (1.5)	0.228
	Difference	-1.3 (2.9)	0.2 (2.4)	-0.8 (3.1)	1.6 (1.9)	0.414	0.6 (2.1)	0.79
Total cholesterol (mg dL ⁻¹)	Soy	196.0 (7.1)	176.7 (5.7)	180.5 (6.2)	-19.3 (4.8)	<.001	-15.5 (4.8)	0.002
	Non-soy	196.9 (7.2)	170.8 (5.8)	182.4 (6.2)	-26.1 (4.8)	<.001	-14.5 (4.7)	0.003
	Difference	-0.9 (10.1)	5.0 (8.2)	-1.9 (8.7)	6.8 (6.8)	0.319	-1.0 (6.7)	0.886
Triglycerides (mg dL ⁻¹)	Soy	122.6 (8.3)	85.3 (4.7)	108.7 (7.6)	-37.3 (7.3)	<.001	-14.0 (8.6)	0.109
	Non-soy	112.4 (8.3)	74.3 (4.8)	91.1 (7.5)	-38.1 (7.23)	<.001	-21.4 (8.5)	0.014
	Difference	10.2 (11.8)	11.0 (6.8)	17.6 (10.6)	0.8 (10.3)	0.94	7.4 (12.1)	0.541
SBP (mmHg)	Soy	115.7 (1.9)	111.5 (2.1)	114.0 (2.4)	-4.3 (2.1)	0.041	-1.7 (2.0)	0.39
	Non-soy	111.1 (2.0)	107.0 (2.1)	110.5 (2.4)	-4.2 (2.1)	0.049	-0.7 (1.9)	0.719
	Difference	4.6 (2.8)	4.5 (2.9)	3.5 (3.4)	-0.1 (2.9)	0.973	-1.0 (2.7)	0.709
DBP (mmHg)	Soy	77.9 (1.3)	74.0 (1.3)	75.4 (1.4)	-3.9 (1.5)	0.013	-2.6 (1.5)	0.1
	Non-soy	73.9 (1.4)	69.9 (1.3)	74.3 (1.4)	-4.0 (1.6)	0.012	0.4 (1.5)	0.79
	Difference	4.0 (1.9)	4.1 (1.8)	1.1 (2.0)	0.1 (2.2)	0.963	-3.0 (2.1)	0.171

¹Intention to treat linear mixed-effects model analysis with unstructured covariance was used to assess the efficacy of intervention on each outcome variable (soy: $n = 36$; non-soy: $n = 35$). Test of time by group interaction was used to test the efficacy of intervention at each time point. Results are mean (standard error). Significant P values ($P < 0.05$) are indicated in bold.

BUN, blood urea nitrogen; CRP, C-reactive protein; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

also contains a significant amount of the amino acid leucine, which has been shown to play a key role in protein synthesis and muscle hypertrophy (26,27). Notably, the critical threshold of daily leucine consumption associated with muscle health is approximately 3 g d^{-1} (28,29), and each of the soy products administered in this trial contained 1.6 g leucine. The results of this trial provide evidence that the consumption of foods high in soy protein is not inferior to other supplemental protein sources when it comes to changes in lean mass observed to occur during volitional weight loss and maintenance. This finding may be especially relevant for vegetarians who may find it difficult to consume enough protein to meet the daily recommended intake of $0.8 \text{ g} \cdot \text{kg} \cdot \text{d}$ and especially that of a high-protein diet ($1.2\text{--}1.6 \text{ g} \cdot \text{kg} \cdot \text{d}$) (30,31).

The regular consumption of soy protein has been associated with improvements in cardiometabolic health

associated with blood lipids and blood pressure (12,32). Although no statistical differences in any of the cardiometabolic outcomes were observed between the soy and non-soy groups (Table 4), there was a trend towards superior improvements in CRP – an inflammatory biomarker of cardiovascular disease risk (33) – in the soy group at the end of M4. These data are in corroboration with those from a similar trial done in older adults (68 ± 5 years) (34) suggesting a possible benefit of a reduced calorie, HP diet with soy on inflammation. Conclusive evidence linking soy food consumption to improvements in cardiovascular health, however, is limited and contradictory because of the high degree of inter-individual variation in the bioavailability and metabolism of the bioactive constituents in soy foods (14).

There are several strengths of this study including block randomization stratified by BMI, age and sex; a reduction in potential bias by using clearly defined

curriculum for all intervention classes in conjunction with classes being taught by the same weight loss coach, in the same room at the same time of day; and the assessment of a wide range of outcome variables following weight loss and a period of self-directed maintenance. In line with other comprehensive behavioural weight loss trials of similar duration, approximately 80% of the participants completed the 4-month weight loss phase of the trial and 63% completed the entire year (35). This is also one of only a few studies that looks specifically at soy protein during weight loss.

The main limitation of the study is the lack of normal protein control groups with and without soy consumption. Such a comparison would allow for a more complete investigation of the relative influences of increased overall protein and soy protein specifically on weight loss and cardiometabolic health. Future researchers should consider these research questions in their study designs. The principal reliance on self-reported food logs for tracking soy and non-soy protein foods is another limitation of the current study. However, the observed increase in BUN is indicative of an overall increase in dietary protein intake, which supports the participants' compliance with the study prescription on a broader level. An unforeseen limitation of the study is the unpreventable use of different methodologies to assess blood lipids at baseline and M12 (VAP and LipoProfile) due to the discontinuation of the VAP method by the laboratory. While overall levels of physical activity were assessed in terms of METs per week, the specific details of exercise intensity and type were not tracked due to the design and approach of the SOS program. Lastly, as with most weight loss studies, participants were predominantly middle aged women (82%), which limit the ability to extrapolate these findings to men and younger or older women.

In conclusion, the results of this study provide evidence that, when consumed as part of a reduced calorie, high-protein diet, soy protein is acceptably comparable in efficacy to other proteins for weight loss among healthy, middle aged adults with overweight/obesity. These findings may be particularly useful to those looking to increase their intake of protein from high-quality, vegetarian sources as part of a high-protein, reduced calorie diet.

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Conflict of Interest Statement

Drs Hill, Wyatt, and Peters have received royalties from the book, *State of Slim*. Dr. Mukherjea is a current employee of DuPont USA and Dr. Flock was previously employed by DuPont USA.

Author Contributions

J. O. H., H. R. W. and J. C. P. conceived the research project; K. J. S., R. D. S. and H. N. conducted the research; K. J. S. and Z. P. performed the statistical analyses; K. J. S. drafted the manuscript, and R. D. S., J. C. P., H. K. N., Z. P., H. R. W., M. R. F., R. M. and J. O. H. provided critical feedback and edits to the manuscript. All authors take responsibility for the final content of the manuscript.

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